PACKAGE LEAFLET

Package leaflet: Information for the user

XEOMIN 50 units powder for solution for injection
XEOMIN 100 units powder for solution for injection
XEOMIN 200 units powder for solution for injection

Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins

Read all of this leaflet carefully before you receive this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What XEOMIN is and what it is used for
2. What you need to know before XEOMIN is used
3. How to use XEOMIN
4. Possible side effects
5. How to store XEOMIN
6. Contents of the pack and other information

1. What XEOMIN is and what it is used for

XEOMIN is a medicine that contains the active substance Botulinum Neurotoxin Type A which relaxes the injected muscles or decreases the salivary flow at the respective administration site.

XEOMIN is used for the treatment of the following conditions in adults

- eyelid spasm (blepharospasm) and spasms affecting one side of the face (hemifacial spasm)
- twisted neck (spasmodic torticollis)
- increased muscle tension/uncontrollable muscle stiffness in shoulders, arms and/or hands (spasticity of the upper limb)
- chronic drooling (sialorrhea) due to neurological disorders.

XEOMIN is used in children and adolescents aged 2 to 17 years and weighing ≥ 12 kg for the treatment of

- chronic drooling (sialorrhea) due to neurological / neurodevelopmental disorders.

2. What you need to know before XEOMIN is used

Do not use XEOMIN

- if you are allergic to Botulinum neurotoxin type A or any of the other ingredients of this medicine (listed in section 6)
- if you suffer from a generalised disorder of muscle activity (e.g. myasthenia gravis, Lambert-Eaton syndrome)
- if you have an infection or inflammation at the proposed injection site.

Warnings and precautions

Side effects may occur from misplaced injections of Botulinum neurotoxin type A temporarily paralysing nearby muscle groups. There have been very rare reports of side effects that may be related to the spread of toxin distant from the injection site to produce symptoms consistent to Botulinum toxin type A effects (e.g. excessive muscle weakness, swallowing difficulties or accidental swallowing of food

or drink into the airways). Patients who receive the recommended doses may experience excessive muscle weakness.

If the dose is too high or the injections too frequent, the risk of antibody formation may increase. Antibody formation can cause treatment with Botulinum toxin type A to fail, whatever the reason for its use.

Talk to your doctor or pharmacist before XEOMIN is used:
- if you suffer from any type of bleeding disorder
- if you receive substances that prevent the blood from clotting (e.g. coumarin, heparin, acetylsalicylic acid, clopidogrel)
- if you suffer from pronounced weakness or decreased muscle volume in the muscle where you will receive the injection
- if you suffer from amyotrophic lateral sclerosis (ALS), which can lead to generalised muscle decrease
- if you suffer from any disease that disturbs the interaction between nerves and skeletal muscles (peripheral neuromuscular dysfunction)
- if you have or have had swallowing difficulties
- if you suffer or have suffered from seizures
- if you have had problems with injections of Botulinum toxin type A in the past
- if you are due to have surgery

Contact your doctor and seek medical attention immediately if you experience any of the following:
- difficulty in breathing, swallowing or speaking
- hives, swelling including swelling of the face or throat, wheezing, feeling faint and shortness of breath (possible symptoms of severe allergic reactions)

Repeated injections with XEOMIN
If you have repeated injections with XEOMIN, the effect may increase or decrease. Possible reasons for this are:
- your doctor may follow a different procedure when preparing the solution for injection
- different treatment intervals
- injections into another muscle
- marginally varying effectiveness of the active substance of XEOMIN
- non-response/therapy failure during the course of treatment

Eyelid spasm (blepharospasm)and spasms affecting one side of the face (hemifacial spasm)
Talk to your doctor before XEOMIN is used, if you:
- have had an eye surgery. Your doctor will then take additional precautions.
- are at risk of developing a disease called narrow angle glaucoma. This disease can cause the inner eye pressure to rise and may lead to a damaging of your optic nerve. Your doctor will know if you are at risk.

During treatment, small punctuated bleedings may occur in the soft tissues of the eyelid. Your doctor can limit these by immediately applying gentle pressure at the injection site.

After you receive a XEOMIN injection into your eye muscle your blinking rate may be reduced. This can lead to a prolonged exposure of the transparent front part of the eye (cornea). This exposure may lead to a damaging of the surface and an inflammation (corneal ulceration).

Twisted neck (spasmodic torticollis)
After the injection you may develop mild to severe swallowing difficulties. This may lead to problems with breathing and you may have a higher risk of inhaling foreign substances or fluids. Foreign substances in your lungs may lead to an inflammation or infection (pneumonia). Your doctor will give you special medical treatment if needed (e.g. in the form of artificial nutrition).

Swallowing difficulties can last for up to two to three weeks after injection, for one patient a duration of up to five months is known.

If you have been inactive for a long period of time, any activity should be started gradually after the XEOMIN injection.

Increased muscle tension/uncontrollable muscle stiffness
XEOMIN can be used to treat increased muscle tension/uncontrollable muscle stiffness in parts of your upper limb, e.g. your arm or hand. XEOMIN is effective in combination with the usual standard treatment methods. XEOMIN should be used together with these other methods.
It is unlikely that this medicine will improve the range of motion of joints where the surrounding muscle has lost its ability to stretch.

If you have been inactive for a long period of time, any activity should be started gradually after the XEOMIN injection.

Chronic drooling (sialorrhea)
Some medicines (e.g. clozapine, aripiprazole, pyridostigmine) may lead to excessive saliva production. First of all the possibility of replacement, reduction or even termination of the inducing medication should be considered before using of XEOMIN as drooling treatment. The use of XEOMIN to reduce medication-induced drooling has not been investigated.

If cases of “dry mouth” develop in association with the administration of XEOMIN your doctor will consider a dose reduction.

When your saliva flow is reduced by XEOMIN, oral health problems such as dental caries may develop or existent problems may further progress. Contact a dentist when starting to use XEOMIN for treatment of chronic drooling. Your dentist may decide to take measures for caries prevention, if needed.

Children and adolescents
Do not give this medicine to children below the age of 2 years, to children weighing less than 12 kg, or to children and adolescents for treatments other than chronic drooling because the use of XEOMIN has not been established in this population and is therefore not recommended.

Other medicines and XEOMIN
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

The effect of XEOMIN may be increased:
- by medicines used to treat certain infectious diseases (spectinomycin or aminoglycoside antibiotics [e.g. neomycin, kanamycin, tobramycin])
- by other medicines that relax the muscles (e.g. muscle relaxants of the tubocurarine-type). Such medicines are used, for example, in general anaesthesia. Before you have surgery, tell your anaesthetist if you have received XEOMIN.
- when used for the treatment of chronic drooling: by other medicines which itself reduce the salivary flow (e.g. anticholinergics as atropine, glycopyrronium or scopolamine) or by therapeutic irradiation to the head and neck, including salivary glands. Tell your doctor if you are receiving radiotherapy or if radiotherapy is planned.

In these cases, XEOMIN must be used carefully.

The effect of XEOMIN may be reduced by certain medicines for malaria and rheumatism (known as aminoquinolines).

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before this medicine is administered.

XEOMIN should not be used during pregnancy, unless your doctor decides that the necessity and potential benefit of the treatment justifies the possible risk on the foetus.

XEOMIN is not recommended if you are breast-feeding.

Driving and using machines
You should not drive or engage in other potentially hazardous activities if drooping eyelids, weakness (asthenia), muscle weakness, dizziness or vision disorders occur.
If in doubt ask your doctor for advice.

3. How to use XEOMIN

XEOMIN may only be administered by doctors with appropriate specialist knowledge of treatment with Botulinum neurotoxin type A.

The optimum dose, frequency and number of injection sites will be chosen by your doctor individually for you. The results of initial treatment with XEOMIN should be evaluated and may lead to dose adjustment until the desired therapeutic effect is achieved. Treatment intervals will be determined by your doctor based on your actual clinical need.

If you have the impression that the effect of XEOMIN is too strong or too weak, let your doctor know. In cases where no therapeutic effect is apparent, alternative therapies should be taken into consideration.

Eyelid spasm (blepharospasm) and spasms affecting one side of the face (hemifacial spasm)
The recommended initial dose is up to 25 units per eye and the total recommended dose in follow-up treatment sessions is up to 50 units per eye. Usually, the first onset of effect is observed within four days after injection. The effect of each treatment generally lasts for about 3-5 months, however, it may last significantly longer or shorter. Treatment intervals of less than 12 weeks are not recommended.

Normally, no additional benefit is conferred by treating more frequently than every three months.

If you suffer from spasm affecting one side of your face (hemifacial spasm) your doctor will follow the treatment recommendations for eyelid spasm (blepharospasm) restricted to one side of the face. The spasm affecting one side of your face (hemifacial spasm) will be treated only in the upper face as injections of XEOMIN in the lower part of the face may lead to increased risk of side effects such as pronounced risk of local weakness.

Twisted neck (spasmodic torticollis)
The recommended dose per single injection site is up to 50 units, and the maximum dose for the first treatment session is 200 units. Doses up to 300 units may be given by your doctor in subsequent courses depending on the response. Usually, the first onset of effect is observed within seven days after injection. The effect of each treatment generally lasts for about 3-4 months, however, it may last significantly longer or shorter. Treatment intervals of less than 10 weeks are not recommended.

Increased muscle tension/uncontrollable muscle stiffness in shoulders, arms or hands (spasticity of the upper limb)
The recommended dose is up to 500 units per treatment session and no more than 250 units should be administered to the shoulder muscles. Patients reported the onset of action 4 days after treatment. An improvement of muscle tone was perceived within 4 weeks. In general, the treatment effect lasted 12 weeks, however, it may last significantly longer or shorter. The period between each treatment session should be at least 12 weeks.

Chronic drooling (sialorrhea, adults)

The recommended dose is 100 units per treatment session. This maximum dose should not be exceeded. The period between each treatment session should be at least 16 weeks.

Chronic drooling (sialorrhea, children/adolescents)
The recommended dose per treatment session depends on body weight. The maximum dose should not exceed 75 units. The period between each treatment session should be at least 16 weeks.

Method of administration
Dissolved XEOMIN is intended for injections into the muscle (intramuscular use) and into salivary glands (intraglandular use) (see information for healthcare professionals at the end of this leaflet). Regarding localization of the salivary glands in adults both anatomic landmarks or ultrasound guidance are both possible; however, the ultrasound guided method should be preferred for efficacy reasons. For children and adolescents, the ultrasound guided method should be used.
Before the injection, children and adolescents may be given a local anaesthetic (such as local anaesthetic cream), sedative or an anaesthetic in combination with a sedative.

If you are given more XEOMIN than you require
Symptoms of overdose:
Symptoms of overdose are not apparent immediately after the injection and may include general weakness, drooping eyelid, double vision, breathing difficulties, speech difficulties, and paralysis of the respiratory muscles or swallowing difficulties which may result in pneumonia.

Measures in cases of overdose:
In case you feel symptoms of overdose please seek medical emergency services immediately or ask your relatives to do so, and have yourself admitted to hospital. Medical supervision for up to several days and assisted ventilation may be necessary.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Usually, side effects are observed within the first week after treatment and are temporary in nature. Side effects may be related to the medicine, injection technique or both. Side effects may be restricted to the area around the injection site (e.g. localised muscle weakness, local pain, inflammation, pins and needles (paraesthesia), reduced sense of touch (hypoaesthesia), tenderness, swelling (general), swelling of the soft tissue (oedema), skin redness (erythema), itching, localised infection, haematoma, bleeding and/or bruising).

The injection of the needle may cause pain. This pain or the anxiety towards needles may lead to fainting, nausea, tinnitus (ringing in the ears) or a low blood pressure.

Side effects such as excessive muscle weakness or swallowing difficulties may be caused by the relaxation of muscles far from the injection site of XEOMIN. Swallowing difficulties can cause inhalation of foreign bodies resulting in lung inflammation and in some cases, death.

An allergic reaction may occur with XEOMIN. Serious and/or immediate allergic reactions (anaphylaxis) or allergic reactions to the serum in the product (serum sickness), causing for example difficulty in breathing (dyspnoea), hives (urticaria) or swelling of the soft tissue (oedema), have been rarely reported. Some of these reactions have been observed following the use of conventional Botulinum toxin type A complex. They occurred when the toxin was given alone or in combination with other medicines known to cause similar reactions. An allergic reaction can cause any of the following symptoms:

- difficulty with breathing, swallowing or speaking due to the swelling of the face, lips, mouth or throat
- swelling of the hands, feet or ankles.

If you notice any of these side effects, please inform your doctor immediately or ask your relatives to do so and go to the accident and emergency department of your nearest hospital.

The following side effects have been observed with XEOMIN.

Eyelid spasm (blepharospasm)
Very common (may affect more than 1 in 10 people):
Drooping eyelid (ptosis)

Common (may affect up to 1 in 10 people):
Dry eyes, vision blurred, visual impairment, dry mouth, injection site pain

Uncommon (may affect up to 1 in 100 people):
Headache, weakness of face muscle (facial paresis), double vision (diplopia), lacrimation increased, swallowing difficulties (dysphagia), fatigue, muscular weakness, rash

Spasms affecting one side of the face (hemifacial spasm)
Similar side effects as for eyelid spasm can be expected when treating spasms affecting one side of the face.

Twisted neck (spasmodic torticollis)
Very common (may affect more than 1 in 10 people):
Swallowing difficulties (dysphagia)

Common (may affect up to 1 in 10 people):
Neck pain, muscular weakness, musculoskeletal pain (myalgia), musculoskeletal stiffness, muscle spasms, headache, dizziness, injection site pain, weakness (asthenia), dry mouth, nausea, sweating increased (hyperhidrosis), upper respiratory tract infection, feeling faint (presyncope)

Uncommon (may affect up to 1 in 100 people):
Speech disorders (dysphonia), shortness of breath (dyspnoea), rash

The treatment of twisted neck may cause swallowing difficulties with varying degrees of severity. This may lead to breathing in foreign materials, which may require medical intervention. Swallowing difficulties may persist for two to three weeks after injection, but has been reported in one case to last five months. Swallowing difficulties appear to be dose-dependent.

Increased muscle tension/uncontrollable muscle stiffness in shoulders, arms or hands (spasticity of the upper limb)
Common (may affect up to 1 in 10 people):
Dry mouth

Uncommon (may affect up to 1 in 100 people):
Headache, reduced sense of touch (hypoaesthesia), muscular weakness, pain in extremity, weakness (asthenia), musculoskeletal pain (myalgia), swallowing difficulties (dysphagia), nausea

Not known (cannot be estimated from the available data):
Injection site pain

Chronic drooling (sialorrhea) in adults
Common (may affect up to 1 in 10 people):
Dry mouth, swallowing difficulties (dysphagia), feeling of pins and needles (paraesthesia)

Uncommon (may affect up to 1 in 100 people):
Thickened saliva, speech disorder, taste disorder (dysgeusia)

Cases of persistent dry mouth (> 110 days) of severe intensity have been reported, which could cause further complications such as gum inflammation (gingivitis), swallowing difficulties and caries.

Chronic drooling (sialorrhea) in children/adolescents
Uncommon (may affect up to 1 in 100 people):
Swallowing difficulties (dysphagia)

Not known (cannot be estimated from the available data):
Dry mouth, thickened saliva, oral pain, dental caries

Post-marketing experience
The following side effects were reported with unknown frequency for the use of XEOMIN since market launch independent from treatment area:
Flu-like symptoms, shrinkage of injected muscle, and hypersensitivity reactions such as swelling, swelling of the soft tissue (oedema, also distant from the injection site), redness, itching, rash (local and generalised), and breathlessness.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the HPRA Pharmacovigilance Website: **www.hpra.ie**. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store XEOMIN

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial label after "EXP". The expiry date refers to the last day of that month.

Unopened vial: Do not store above 25 °C.
Reconstituted solution: Chemical and physical in-use stability has been demonstrated for 24 hours at 2 °C to 8 °C.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

Your doctor should not use XEOMIN if the solution has a cloudy appearance or contains visible particles.

For instructions on disposal, please see information for healthcare professionals at the end of this leaflet.

6. Contents of the pack and other information

What XEOMIN contains

- The active substance is: Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins.
  XEOMIN 50 units powder for solution for injection
  One vial contains 50 units of Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins*.
  XEOMIN 100 units powder for solution for injection
  One vial contains 100 units of Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins*.
  XEOMIN 200 units powder for solution for injection

One vial contains 200 units of Clostridium Botulinum neurotoxin type A (150 kD), free from complexing proteins*.
** Botulinum neurotoxin type A, purified from cultures of Clostridium Botulinum (Hall strain)*

- The other ingredients are: human albumin, sucrose.

What XEOMIN looks like and contents of the pack
XEOMIN is presented as a powder for solution for injection. The powder is white. Reconstituting the powder produces a clear, colourless solution.

XEOMIN 50 units powder for solution for injection: Pack sizes of 1, 2, 3 or 6 vials
XEOMIN 100 units powder for solution for injection: Pack sizes of 1, 2, 3, 4 or 6 vials
XEOMIN 200 units powder for solution for injection: Pack sizes of 1, 2, 3, 4 or 6 vials

Not all pack sizes may be marketed.

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This medicine is authorised in the Member States of the European Economic under the following names:

XEOMIN:	Austria, Bulgaria, Cyprus, Croatia, Czech Republic, Denmark, Estonia, Germany, Greece, Finland, France, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden
XEOMEEN:	Belgium

This leaflet was last revised in {MM/ YYYY}.

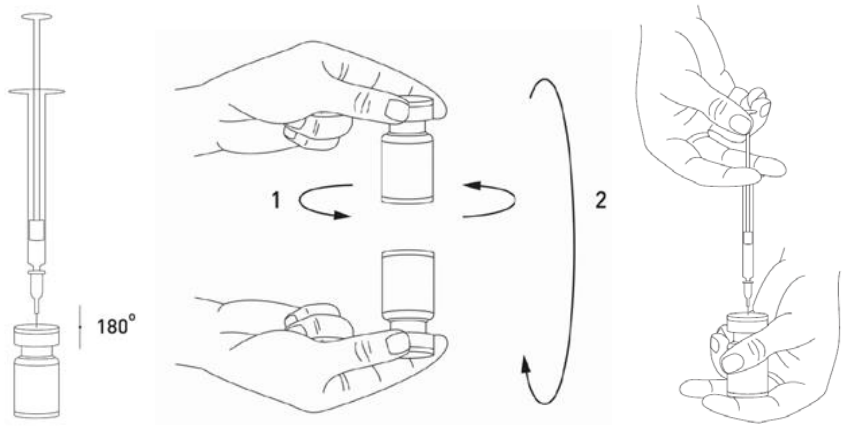
The following information is intended for healthcare professionals only:

Instructions for reconstitution of the solution for injection:
XEOMIN is reconstituted prior to use with sodium chloride 9 mg/ml (0.9 %) solution for injection.

XEOMIN may only be applied for its intended use to treat one patient for one session.

It is good practice to reconstitute the vial contents and prepare the syringe over plastic-lined paper towels to catch any spillage. An appropriate amount of sodium chloride solution (see dilution table) is drawn up into a syringe. A 20-27 G short bevel needle is recommended for reconstitution. After vertical insertion of the needle through the rubber stopper, the solvent is injected gently into the vial in order to avoid foam

formation. Discard the vial if the vacuum does not pull the solvent into the vial. Remove the syringe from the vial and mix XEOMIN with the solvent by carefully swirling and inverting/flipping the vial – do not shake vigorously. If needed, the needle used for reconstitution should remain in the vial and the required amount of solution should be drawn up with a new sterile syringe suitable for injection.



Reconstituted XEOMIN is a clear, colourless solution.

XEOMIN must not be used if the reconstituted solution (prepared as above) has a cloudy appearance or contains floccular or particulate matter.

Care should be taken to use the correct solvent volume for the presentation chosen to prevent accidental overdose. If different vial sizes of XEOMIN are being used as part of one injection procedure, care should be taken to use the correct amount of solvent when reconstituting a particular number of units per 0.1 ml. The amount of solvent varies between XEOMIN 50 units, XEOMIN 100 units and XEOMIN 200 units. Each syringe should be labelled accordingly.

Possible concentrations for XEOMIN 50, 100 and 200 units are indicated in the following table:

Resulting dose in units per 0.1 ml	**Solvent added** (sodium chloride 9 mg/ml (0.9 %) solution for injection)		
	Vial with 50 units	**Vial with 100 units**	**Vial with 200 units**
20 units	0.25 ml	0.5 ml	1 ml
10 units	0.5 ml	1 ml	2 ml
8 units	0.625 ml	1.25 ml	2.5 ml
5 units	1 ml	2 ml	4 ml
4 units	1.25 ml	2.5 ml	5 ml
2.5 units	2 ml	4 ml	Not applicable
2 units	2.5 ml	5 ml	Not applicable
1.25 units	4 ml	Not applicable	Not applicable

Instructions for disposal
Any solution for injection that has been stored for more than 24 hours as well as any unused solution for injection should be discarded.

Procedure to follow for a safe disposal of vials, syringes and materials used
Any unused vials or remaining solution in the vial and/or syringes should be autoclaved. Alternatively, the remaining XEOMIN can be inactivated by adding one of the following solutions: 70 % ethanol, 50 % isopropanol, 0.1 % SDS (anionic detergent), diluted sodium hydroxide solution (0.1 N NaOH), or diluted sodium hypochlorite solution (at least 0.1 % NaOCl).

After inactivation used vials, syringes and materials should not be emptied and must be discarded into appropriate containers and disposed of in accordance with local requirements.

Recommendations should any incident occur during the handling of Botulinum toxin type A

- Any spills of the product must be wiped up: either using absorbent material impregnated with any of the above solutions in case of the powder, or with dry, absorbent material in case of reconstituted product.
- The contaminated surfaces should be cleaned using absorbent material impregnated with any of the above solutions, then dried.
- If a vial is broken, proceed as mentioned above by carefully collecting the pieces of broken glass and wiping up the product, avoiding any cuts to the skin.
- If the product comes into contact with skin, rinse the affected area abundantly with water.
- If product gets into the eyes, rinse thoroughly with plenty of water or with an ophthalmic eyewash solution.
- If product comes into contact with a wound, cut or broken skin, rinse thoroughly with plenty of water and take the appropriate medical steps according to the dose injected.

These instructions for use, handling and disposal should be strictly followed.